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Comparison of Respiratory Distress Syndrome (RDS) between Gestational Age 34 Weeks and 35-36 Weeks

Rarin Imkesorn, MD*,
Wiyada HLuangdansakul, MD*,
Sinart Prommas, MD*,
Anuruk Chotedelok*,
Thiansiri Luangwilai*.

** Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Bangkok 10220, Thailand*

ABSTRACT

Objective: To compare the incidence of respiratory distress syndrome (RDS) in late preterm infants at gestational age of 34 weeks and 35-36 weeks and also to compare the rates of short term neonatal complications among infants at gestational age of 34, 35-36 weeks and term (37-40 weeks).

Materials and Methods: This study was a retrospective cohort design. Two hundred late preterm (99 cases for GA 34 weeks and 101 cases for GA of 35-36 weeks) and 100 normal term neonates were recruited. RDS and short-term complications in neonates who were born at the Bhumibol Adulyadej Hospital from January 2011 to June 2014 were compared. The data were analyzed with Chi-square test, Student's t-test and analysis of variance where appropriate.

Result: RDS rate was higher in the late preterm group with GA 34-$34^{6/7}$ weeks than in the group with GA 35-$36^{6/7}$ weeks (15% and 4.0% respectively with $p = 0.015$). There was no RDS in normal term (GA 37-40 weeks) babies. The short-term complications: oxygen requirement, hyperbilirubinemia, hypoglycemia, hypothermia, NICU admission and hospital stay were also higher in 34-$34^{6/7}$ week gestation group.

Conclusion: The incidence of RDS is significantly higher in late preterm with GA 34-$34^{6/7}$ weeks than other groups.

Keywords: Respiratory distress syndrome, Respiratory complication

Introduction

Late preterm is defined as infants who are born at 34 to 36 weeks of gestatio. Almost 13% of infants in the united states are born preterm, and more than 70% of them were late preterm[1]. The incidence of late-preterm births has increased by 25% since 1990[1]. In Thailand, the number of babies borned before 37 completed weeks has been rapidly increase. The majority of this group is late preterm (about 72%) and it tends to keep on increasing.

Late preterm birth is associated with prematurity-associated short-term morbidities, especially respiratory distress syndrome which required special care and prolonged neonatal hospital stays. Recent studies of

late-preterm infants have documented increased short term and long term morbidities when compared to full term infants[2]. Short term morbidities include respiratory distress syndrome (RDS), hypothermia, hypoglycemia, hyperbillirubinemia, feeding difficulties and bacterial infection. The American College of Obstetricians and Gynecologist recommends delivery for preterm PROM be conducted at 32-33 completed weeks, with positive fetal lung maturity testing, or at ≥ 34 weeks[3]. Similarly, recent cohort suggests that prolongation of preterm PROM beyond 34 weeks has limited benefits[4]. Several retrospective studies in the past decade found strong association between RDS and gestational age at delivery[5-6].

The incidence of respiratory distress syndrome was 10.5% for infants who were born at 34 weeks gestation and 0.3% at 38 weeks. Similarly, the incidence of transient tachypnea of the newborn was 6.4% for those who were born at 34 weeks and 0.4% at 38 weeks, pneumonia was 1.5% vs 0.1% and respiratory failure was 1.6% vs 0.2% respectively[7]. Some RDS infants require mechanical ventilation depending on the degree of prematurity, whereas 3.3% of infants born at 34 weeks need assisted ventilation[8]. However evidence showed that the rate of short-term respiratory complications of late preterm newborns were higher than those at term[9]. Few studied examined the differences of respiratory morbidities among late preterm with different gestational age. However, the data were limited due to small sample number[2,4-6].

Preterm cases accounted for at least 10% of all deliveries at Bhumibol Adulyadej hospital. The shortage of NICU beds and respirators are always problematic. Decreasing the rate of infant with RDS would lower the NICU admission and respiratory support. To determine the complication of these late preterm neonates in different gestation is important for clinical decision.

Materials and Methods

This retrospective cohort study was approved by the Institutional Review Board of Bhumibol Adulyadej Hospital. The inclusion criteria were infants delivered at the Bhumibol Adulyadej Hospital between January 2011 and June 2014. The exclusion criteria were multifetal gestations, infants with major anatomic malformations, fetal demise, infants received antenatal corticosteroid therapy, infants referred from another health care units and infants born from mothers who received no antenatal care or had antenatal care for less than 4 times. All medical records of infants borned at ≥ 34 completed weeks to $36^{6/7}$ weeks were reviewed. Medical records of mother-infant who delivered at 37 to 40 completed weeks of gestation in the same time period were systematic randomly selected. Gestational age was based on the first day of last menstrual period (LMP) and confirmed by either first or second trimester scan. A normal LMP was defined as regular period without antecedent oral contraceptive use. In the first trimester, gestational age was based on cown-lump–length measurements. Gestational age in the sesond trimester was comfirmed by measurements of BPD, HC, AC, and FL[18].

Major neonatal morbidities associated with late-preterm infants were analyzed. The selected individual outcomes were respiratory distress syndrome (RDS), pneumonia, oxygen requirement, hypoglycemia, required phototherapy hyperbillirubinemia, neonatal congenital sepsis. RDS was defined tachypea develops, the chest wall retracts and expiration is accompanied by grunting and nostril flaring. The chest radiograph shows a diffuse reticulogranular infiltrate and airbronchogramon chest[10]. Pneumonia by presence of abnormal signs on physical examination consistent with pulmonary diseases, abnormal chest radiograph with nonhomogeneous finding, and a high clinical suspicious for infection. The chest radiograph can confirm the clinical diagnosis of pneumonia. Bilateral alveolar densities with air bronchograms are characterised[11], but irregular patchy infiltrates or occasionally a normal pattern may also occur[12]. Transient trachypnea of the newborn (TTN) is a clinical diagnosis. Characteristic findings on chest radiograph support the diagnosis. These include increased lung volumes with flat diaphragms, mild cardiomegaly, and prominent vascular markings in a sunburst pattern originating at the hilum. Fluid often is seen in the interlobar fissures, and pleural effusions may be

present. Alveolar edema may appear as fluffy densities[13].

Sample size was calculated to detect a clinically relevant difference of RDS rate with a 7% difference between infants born at gestational age 34 weeks and 35-36 weeks. A statistical power of 95% and significant level of 5% was selected. The 7% difference between groups was estimate from a previous study; a systemic review of severe morbidity in infants born late preterm[15]. Sample size was estimated to be at least 95 per group. Categorical values were compared by the Pearson chi-square test. Continuous data was compared using ANOVA analysis.

$$N = \frac{\{Z\alpha\sqrt{2pq} + Z\beta\sqrt{P1[1+R-P1(1+R^2)]}\}^2}{[P1(1-R)]^2}$$

$Z\alpha$ = 95% confidence interval
(Type I error, Two tailed) = 1.96
$Z\beta$ = Type II error power 10% = 1.28

Patients were identified by terminology codes to create a list of all mothers delivered between January 2011 and June 2014. Newborn data were obtained by accessing the newborn records for those women. All patients data were taken from Bhumibol Adulyadej hospital computer patient database. The complete scanned handwritten records for every patient from admission to discharge were reviewed to confirm diagnoses by attending obstetricians and pediatricians. Data on respiratory support such as oxygen therapy administered through nasal-cannula (nasal oxygen), nasal continuous positive airways pressure (N-CPAP), mechanical ventilation, (MV) were collected. According to departmental protocol, respiratory support was provided by nasal oxygen or N-CPAP for the first signs of respiratory impairment. MV was limited to those infants who did not response to N-CPAP or those who need resuscitation. They were extubated as soon as possible and N-CPAP was then applied. Data of the highest level of respiratory support was collected. Outcome data were compared among neonates born at $34^{0/7}$ to $34^{6/7}$ weeks, at $35^{0/7}$ to $36^{6/7}$ weeks and at $37^{0/7}$ to $40^{0/7}$ weeks. All infants were followed up until discharge.

Results

There were 11,385 deliveries during 2011-2014. There were 1,207 (10.6%) preterm deliveries and 911 of them were late-preterm (75% of preterm birth). During the study period, 300 women with their infants met the eligibility criteria and had completed maternal and neonatal medical records information required for analysis. Demographic data (Table 1), including maternal age, sex of infants, indications for delivery were not significant different among the three groups (34 weeks gestation, 35-36 weeks gestation, term (37-40 weeks). The most common indication for delivery was spontaneous labor (81%, 86%, 90.6%). The second most common indication was hypertensive disorder (11% in 34 weeks gestation group, 9.9% in 35-36 weeks gestation group). (Table 2)

Neonatal RDS was strongly associated with gestational age at delivery. The RDS rate was significantly higher in 34 weeks neonate comparing with the 35-36 weeks gestation and the 37-40 weeks gestation (15.0%, 4.0% and 0.9% respectively). There are three different kinds of respiratory complications; RDS, TTN and pneumonia. RDS was the most common complication and more common the 34 weeks neonates. Oxygen requirement was significantly higher.

Thirty-two late preterm infants (16%) and 1 term infant (0.9%) received respiratory intervention. Six late preterm infants (1.2%) and none of term infant were ventilated. Infants at 34 week gestational group require intubation 5 times more than infants at 35-36 week gestational. (Table 3)

Table 1. Demographic and Perinatal Variables

	GA $34^{0/7}$-$34^{6/7}$ n=99	GA $35^{0/7}$-$36^{6/7}$ n=101	GA $37^{0/7}$-40 n=100	χ^2	P
Infant sex					
Male	56	56	64	1.79	0.41
Female	43	45	36		
Maternal age					
< 20 yrs	3	10	4		
20 - 24	18	24	25		
25 - 29	25	25	27	12.9	0.115
30 - 34	28	27	23		
≥ 35	25	15	21		

Table 2. Indications of Delivery

Indication	GA $34^{0/7}$-$34^{6/7}$ n	GA $35^{0/7}$-$36^{6/7}$ n	GA $37^{0/7}$-40 n	χ^2	P
Spontaneous	80	87	97	14.9	0.247
Hypertensive Disorder	11	10	2		
Non reassuring Fetus	3	1	2		
Abruptio Placenta	0	1	0		
PROM > 18 hr.	1	0	2		
Placenta Previa	3	1	1		
IUGR	1	1	0		

Table 3. Respiratory Complications

Respiratory Complications	GA $34^{0/7}$-$34^{6/7}$ n (%)	GA $35^{0/7}$-$36^{6/7}$ n (%)	GA $37^{0/7}$-40 n (%)	χ^2	P
RDS	15 (15.0)	4 (4.0)	1 (0.9)	21.35	0.000
TTN	6 (6.0)1	6 (5.9)	0	1.79	NS
Pneumonia	1 (0.01)	0	0		NS
Oxygen requirement					0.000
intubation	5	1	0		
nasal CPAP	9	3	0		
Oxygen box	8	6	1		
Total	22	10	1		

The other neonatal outcomes are presented in Table 4. including hyperbilirubinemia, hypoglycemia, hypothermia, sepsis, NEC, IVH. Hypoglycemia was the most common complication, followed by hyperbillirubinemia. The incidence of hypoglycemia was significantly higher in 34 week gestational (51%) than those of 35-36 week gestation and term (27.7% and 6.5% respectively).

NICU admission and hospital stay are presented in Table 5. The NICU admission rate in late preterm infants had significant higher than term infants. It was slightly higher in 34 gestational group than the 35-36 gestational week group (36% and 31.7%) but this difference was not statistically significant. NICU admission was 4.7% in term infants, The number of infants born at 34 week gestation admitted to NICU more than 5 days was 80.6%. It was 64.5% in infant born at 35-36 week. The average length of hospital stay in preterm infants in 34 week gestational age group was longer than the infants in the age group of 35-36 weeks (5.55 ± 6.20 days, 4.8 ± 4.62 respectively).

Table 4. Other Neonatal Outcome

Neonatal complication	GA $34^{0/7}$-$34^{6/7}$ n (%)	GA $35^{0/7}$-$36^{6/7}$ n (%)	GA $37^{0/7}$-40 n (%)	χ^2	P
Hyperbilirubinemia	38 (38.0)	31 (30.7)	9 (9)	0.00	0.247
Hypoglycemia	51 (51.0)	28 (27.7)	7 (6.5)	0.00	
Hypothermia	6 (6.0)	7 (6.9)	0 (0)	0.026	
Sepsis	5	4	1	NS	
NEC	1	0	0	NS	
IVH	0	0	0	NS	

Table 5. NICU admission and hospital stay

Neonatal complication	GA $34^{0/7}$-$34^{6/7}$ n (%)	GA $35^{0/7}$-$36^{6/7}$ n (%)	GA $37^{0/7}$-40 n (%)	P
NICU	36 (36)	31 (31.7)	5 (4.7)	0.000
NICU > 5 days	29 (80.6)	20 (64.5%)	2 (40)	0.000
Hospital stay	5.55 ± 6.201	4.8 ± 4.626	2.83 ± 1.356	0.000

Discussion

This study showed that late-preterm infants can develop important short-term neonatal morbidity. Previous studies have shown that late-preterm infants have a high rate of neonatal complication: oxygen requirement, hyperbilirubinemia, hypoglycemia, hypothermia, NICU admission. In this study we found that the RDS was the more common in neonate born at gestational age 34-$34^{6/7}$ comparing to GA $35^{0/7}$-$36^{6/7}$ and GA $37^{0/7}$-40.

This retrospective study excluded 32 late preterm births Most of them were because of uncertain gestational age. Prospective design with accurate gestational age will be useful.

The association of increased rates of respiratory morbidity in lower gestational age was detected which is similar to those of Yoder BA. and colleagues[14], Teune MJ, et al[15], but different from Mateus Julio, et al[5]. The overall incidence of RDS was 6.6% which similar Lubow JM[6], Naef RW. et al[16]'s studies The incidence of RDS

in infant born at 34 weeks gestation and 35-36 weeks gestation were 15%, 3.9% respectively. It was higher comparing to study from Teune MJ. et al[15], (15% vs 10.5%). The incidence of RDS in infant born at 35-36 week gestation was similar (4.0% vs 3.8%). It was was nearly 4-fold higher in infant 34-34$^{6/7}$ gestational age than in the 35-36 gestational age groups. RDS was the most common complication (9.5%) in the late preterm, followed by TTN (6%). This finding was higher than study from Nir Melamed[17] (4.2% for RDS, 8.6% for TTN). These may be because ofthe heterogeneity of studies, selection criteria and definition of the outcomes. Despite the rigorous definitions used to describe RDS and TTN, the diagnosis may still be subjective and the distinction between TTN and RDS may be unclear.

Jaundice was the most common short term neonatal outcome. The second most common was hypoglycemia and the third was RDS. The highest admission rate to the NICU and the longest hospitals stay also occurred in newborns at 34 weeks. More than one third of these infants were admitted to the NICU and moreover 80.6% were admitted to the NIUC more than 5 days. However the admission rate to the NICU in newborns at 34 week was not significant higher than those born at 35-36 weeks. The NICU admission rate more than 5 days was more common in 34 weeks group when compared to 35-36 weeks group (80.6% and 64.5% respectively). Hyperbilirubinemia that required phototherapy was the most common minor complication occurred 51%, 27.7%, 6.5% in neonate born at 34 weeks, 35-36 weeks and 37-40 weeks. Specific neonatal short term clinical outcomes differed significantly at 34 weeks as compared to 35-36 weeks were observed in a recent cohort.

The neonatal complications in late preterm birth were more common in GA 34 to 34$^{6/7}$ than GA from 35 complete weeks. This is difference from our knowledge that the prognosis is good if the pregnancy passes 34 complete weeks gestation. When obstetricians faced preterm labor, the important thing to keep in mind is that the more gestational age, the less neonatal complications.

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References

1. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Mathews TJ, Osterman MJK. Births: final data for 2008.National Vital Statistic Reports 2010;59:13–71.
2. Bastek JA, Sammel MD, Paré E, Srinivas SK, Posencheg MA, Elovitz MA. Adverse neonatal outcomes: examining the risks between preterm, late preterm, and term infants. Am J Obstet Gynecol 2008;199:367–8.
3. ACOG Practice Bulletin No. 107. Induction of labor. Obstet Gynecol 2009;114:386–97.
4. Lieman JM, Brumfield CG, Carlo W, Ramsey PS. Preterm premature rupture of membranes: is there an optimal gestational age for delivery? Obstet Gynecol 2005;105:12–7.
5. Mateus J, Fox K, Jain S, Jain S, Latta R, Cohen J. Preterm premature rupture of membranes: clinical outcomes of late-preterm infants. Clin Pediatr 2010;49:60–5.
6. Lubow JM, How HY, Habli M, Maxwell R, Sibai BM. Indications for delivery and short-term neonatal outcomes in late preterm as compared with term births. Am J Obstet Gynecol 2009;200:30–3.
7. Consortium on Safe Labor, Hibbard JU, Wilkins I, Sun L, Gregory K, Haberman S, et al. Respiratory morbidity in late preterm births. JAMA 2010;304:419–25.
8. McIntire DD, Leveno KJ. Neonatal mortality and morbidity rates in late preterm births compared with births at term. Obstet Gynecol 2008;111:35–41.
9. Sun H, Xu F, Xiong H, Kang W, Bai Q, Zhang Y, et al. Characteristics of respiratory distress syndrome in infants of different gestational ages. Lung 2013;191:425–33.
10. ACOG Practice Bulletin No. 97. Fetal lung maturity. Obstet Gynecol 2008;112:717–26.
11. Brook I, Martin WJ, Finegold SM. Bacteriology of tracheal aspirates in intubated newborn. A radiologic update on medical diseases of the newborn. Chest 1980;78:875–7.
12. Cleveland RH. A radiologic update on medical diseases of the newborn chest. Pediatr Radiol 1995;25:631–7.
13. Avery ME, Gatewood OB, Brumley G. Transient tachypnea of newborn. Possible delayed resorption of fluid at birth. Am J Dis Child 1966;111:380–5.
14. Yoder BA, Gordon MC, Barth WH. Late-preterm birth: does the changing obstetric paradigm alter the epidemiology of respiratory complications?. Obstet Gynecol 2008;111:814–22.
15. Teune MJ, Bakhuizen S, Gyamfi Bannerman C, Opmeer BC, van Kaam AH, van Wassenaer AG, et al. A systematic review of severe morbidity in infants born late preterm. Am J Obstet Gynecol 2011;205:374–9.

16. Naef RW, Allbert JR, Ross EL, Weber BM, Martin RW, Morrison JC. Premature rupture of membranes at 34 to 37 weeks' gestation: aggressive versus conservative management. Am J Obstet Gynecol 1998;178:126–30.
17. Melamed N, Klinger G, Tenenbaum-Gavish K, Herscovici T, Linder N, Hod M, et al. Short-term neonatal outcome in low-risk, spontaneous, singleton, late preterm deliveries. Obstet Gynecol 2009;114:253–60.
18. Kalish RB, Chervenak F. Sonographic determination of gestational age. TMJ 2009;59:202-8.

เปรียบเทียบอัตราการเกิดภาวะระบบทางเดินหายใจล้มเหลว (Respiratory Distress Syndrome) ในทารกคลอดก่อนกำหนดอายุครรภ์ 34 สัปดาห์ และ อายุครรภ์ 35 ถึง 36 สัปดาห์

รริน อิ่มเกษร, วิยะดา เหลืองด่านสกุล, ศินาท พรหมมาศ, อนุรักษ์ โชติดิลก, เทียนศิริ เหลืองวิไล

วัตถุประสงค์ *: การศึกษานี้เพื่อเปรียบเทียบอัตราการเกิดภาวะทางเดินหายใจล้มเหลวในทารกแรกคลอด ในทารกคลอดก่อนกำหนดในช่วงอายุครรภ์ 34 สัปดาห์, 35-36 สัปดาห์ และทารกคลอดครบกำหนด (37-40 สัปดาห์) และเปรียบเทียบภาวะแทรกซ้อนของทารกแรกคลอดระหว่างทารก 3 กลุ่มข้างต้น*

วัสดุและวิธีการ *: งานวิจัยนี้เป็นการศึกษาแบบ retrospective cohort analysis โดยเก็บข้อมูลย้อนหลังของทารกแรกเกิดที่คลอดในโรงพยาบาลภูมิพลอดุลยเดช จาก มกราคม 2554 จนถึง มิถุนายน 2557 โดยแบ่งทารกออกเป็น 3 กลุ่ม กลุ่มแรกคือทารกที่คลอดเมื่ออายุครรภ์ 34 สัปดาห์ กลุ่มที่สองคือทารกอายุครรภ์ 35 – 36 สัปดาห์ และกลุ่มทารกคลอดครบกำหนด*

ผลการศึกษา *: พบว่าภาวะอัตราการเกิดภาวะระบบทางเดินหายใจล้มเหลวพบมากที่สุดในกลุ่มทารกคลอดก่อนกำหนดอายุครรภ์ 34 สัปดาห์ อย่างมีนัยสำคัญทางสถิติเมื่อเปรียบเทียบกับทารกที่คลอดเมื่ออายุครรภ์ 35-36 สัปดาห์ และทารกคลอดครบกำหนด*

สรุป *: อัตราการเกิดภาวะระบบทางเดินหายใจล้มเหลว ในทารกแรกคลอดสัมพันธ์กับอายุครรภ์ โดยพบว่ายิ่งอายุครรภ์น้อยยิ่งพบภาวะนี้ได้มาก โดยเมื่อเปรียบเทียบกันในกลุ่มของทารกคลอดใกล้ครบกำหนด พบว่าทารกที่คลอดเมื่ออายุครรภ์ 34 สัปดาห์ พบอัตราการเกิดภาวะระบบหายใจล้มเหลวมากกว่าทารกในกลุ่มอื่นๆ อย่างมีนัยสำคัญทางสถิติ*